

**REMARKS**

Claims 26-32, 34-40 and 42 are pending. No claims are added, amended, or canceled.

Claims 26-29, 32, 34-40, and 42 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over of U.S. Patent No. 5,514,789 ("the Kempe patent") in view of U.S. Patent No. 5,847,105 ("the Baldeschwieler patent"). Applicants submit that the Office Action does not establish that the claimed invention would have been obvious. To establish a *prima facie* case for obviousness, the following elements must be shown:

- (1) the reference(s) is (are) available as prior art against the claimed invention;
- (2) the motivation (explicit or implicit) provided by the reference(s) that would have rendered the claimed invention obvious to one of ordinary skill in the art at the time of the invention;
- (3) a reasonable expectation of success;
- (4) the basis for concluding that the claimed invention would have been obvious to do, not merely obvious to try; and
- (5) the reference(s) teach(es) the claimed invention as a whole.

The instant Office Action fails to establish at least elements 2 to 4. Hence, a rejection for alleged obviousness is improper. *In re Grabiak*, 769 F.2d 729, 733, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1983).

As admitted in the Office Action (page 3), the Kempe patent does not teach jetting solutions onto the support. There is nothing to motivate one skilled in the art to combine the cited art to overcome this deficiency.

As a general principle those skilled in the art would not look to import into a first teaching a device from a second teaching that is incapable of performing the essential function of the first teaching. The essential function disclosed in the Kempe patent is to use a gas phase reaction for cleavage and deprotection of newly synthesized oligonucleotides. The Baldeschwieler patent uses an ink jet like device for "jetting" reagents including cleavage / deprotection reagents. As is well known, jetting devices are only compatible for use with solution phase reactions and are not compatible for use with gaseous phase reactions. Thus, irrespective of any other teachings of the Kempe and Baldeschwieler patents, one skilled in the art would not look to import into the method of the Kempe patent a device from the

Baldwswieler patent that is incapable of performing the essential function of the disclosure of the Kempe patent.

The Office appears to suggest the combination of art solely “because of the advantages of performing multiple reactions on the same support as taught by Baldeschwieler” (page 4 of the Office Action). The Kempe patent, however, already teaches using multiple reactions and suggests the use of 96 well microliter plates (see the Kempe patent at column 2, line 64). Thus, the Kempe patent already performs multiple reactions on the same support. Because such teachings are already included in the Kempe patent, there is no motivation for one skilled in the art to utilize the teachings of the Baldeschwieler patent.

Without a motivation to combine the cited art, there can be no reasonable expectation of success in such a combination. Without a motivation to combine, at most the combination of the cited art would be obvious to try, not obvious to do.

Furthermore, combining the cited art will not produce any instantly claimed invention. The last step of applicant’s independent claims 26 and 38 both require “jetting onto those reaction sites ...a further chemical reactant species comprising a cleaving reagent to effect cleavage of the reactions product from the reaction support.” The Kempe patent’s gaseous phase reagent is a cleavage/deprotection reagent (see the Kempe patent at column 2, line 42). As noted above, the Kempe patent’s gaseous phase is incompatible with Baldeschwieler’s jetting apparatus. Thus, even if the Kempe and Baldeschwieler patents were combined, they do not produce any claimed invention. Applicant’s submit that applicant’s claims are not obvious in view of the combination of the Kempe and Baldeschwieler patents.

Claims 26-27, 29, 32, 34-40 and 42 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,031,074 (“the Saxinger patent”) in view of the Kempe patent, the Baldeschwieler patent and Salmon, *et al*, *Proc. Nat. Acad. Sci. USA* **1993**, 90, 11708-11712 (“the Salmon reference”). Applicants submit that the Office has not established a *prima facie* case of obviousness.

The combination of cited art does not produce any claimed invention. As admitted by the Office Action (page 5), the reservoir of the Saxinger patent is an indentation, impression, cavity, sunken area or the like. Such a reservoir is not a first and second surface including a plurality of reaction wells in fluid communication with each of a first and a second surfaces

as is required by applicant's independent claim 26 or a first surface and a second surface where the first and second surfaces are substantially parallel to one another and wherein the reaction support is present in subportions located with reaction wells as is required by applicant's claim 38. The Office Action (page 5) points to a disclosure of an inward facing surface of the Saxinger patent is "activated for the attachment (or anchoring) of a ... amino acid" (or for argument sake only for some other compound) but this disclosure does not constitute a reaction well between two surfaces to allege disclosure to the reaction wells of the instant claims. At most, this disclosure is of a reaction well in one surface, not two as recited in the claims.

The Office Action (the last two lines of text on page 5 of the Office Action) states that at page 23, lines 14-21, the Saxinger patent teaches "alternative systems including beads and porous filters" (col. 12, lines 39-45 of the issued patent). This, however, is not the complete teachings of the above quoted passage which reads: "[w]hile alternative systems might easily be based on beads, rods, open flexible tubing, porous filters, etc., the value of using microtiter plates or clusters of tubes in a microtiter format was the existence of commercially available robotic workstations which could be used to automate the cyclinical transfer of reagents in and out of reservoirs in a chosen substrate." Given the totality of the text at page 23, line 14-21 of the Saxinger patent, it is submitted the art skilled would be appraised that using microtiter plates in place of beads or porous filters is advantageous because microtiter plates or clusters of tubes in a microtiter format is useful in commercially available robotic workstations for automation of cyclinical transfer of reagents in and out of reservoirs. Thus the art skilled would be lead away from "beads or porous filters."

Further, claim 1 of the Saxinger patent teaches in step (a) of this claim "one or more reservoirs ... wherein each of said reservoirs opens on a single surface of said substrate..." (the Saxinger patent at column 2, lines 3-5). This is in contrast to the claims under examination that require a first and a second surface not a single surface. Thus, rather than rendering applicant's claims obvious, the Saxinger patent teaches away for a critical feature of applicant's claims. Nothing in the other cited art cures this defect.

There is no motivation to combine the teachings of the Baldeschwieler patent with the teachings of the Saxinger patent. The Office Action (page 6) notes that the Saxinger patent does not teach jetting. Rather, the Saxinger patent teaches using a robot for dispensing

reagents. Indeed, as is noted above, use of microtiter plates is taught by the Saxinger patent to be advantageous because they can be used with commercially available robotic workstations for automation of transfer of reagents. Given the advantages noted in the Saxinger patent of such robotic workstations, one skilled in the art would not ignore these teachings in the Saxinger patent and substitute the jetting apparatus of the Baldeschwieler patent. Quite to the contrary, the art skilled is taught just the opposite – it is advantageous to use robotic workstations. Thus, the art skilled would not incorporate the dispensing means of the Baldeschwieler patent given that the Saxinger patent praises its robotic workstation devices.

Given the lack of first and second surfaces, as is required by applicant's claims, the Saxinger patent, alone or in combination with the Baldeschwieler patent, the Kempe patent and the Salmon reference does teach or suggest any claimed invention. Given that the Saxinger patent's explicit teaching of the advantageous use of robotic workstations, contrary to modifying the Saxinger patent as per the teachings of the Baldeschwieler patent, the art skilled would be very hesitate to modify this advantageous component of the Saxinger patent. There is nothing in the Kempe patent or the Salmon reference that cures this deficiency. Applicant's submit that applicant's claims are not obvious in view of the combination of the cited art.

Claims 28 and 30-31 are rejected stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over the Saxinger patent in view of the Kempe patent, the Baldeschwieler patent and the Salmon reference and U.S. Patent No. 4,923,901 ("the Koester patent"). Applicants submit that the Office has not established a *prima facie* case of obviousness.

As discussed above, the Saxinger patent does not teach reaction wells in fluid communication with a first and a second surface. Thus, the use of these specific supports was not known in combination with supports having first and second surfaces that have reaction wells connecting these surfaces and additionally such supports used in combination with jetting of reagents in to the reaction wells that extend between these support surfaces. Nothing in the Koester patent cures this defect. Thus, even if one were to combine the teachings of the Koester patent with the Saxinger patent, the Baldeschwieler patent and the Salmon reference, one would not arrive at any claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection.

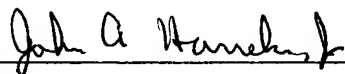
**DOCKET NO.:** ISIS-4766  
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**PATENT**

The foregoing is believed to constitute a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of all of pending claims is earnestly solicited.

Respectfully submitted,

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